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## , What is claimed is:

1. A method for ligating a first oligopeptide with a second oligopeptide end to end for producing an oligopeptide product, the method comprising the following steps:

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Step A: admixing the first and second oligopeptides in a reaction solution including a catalytic thiol, the first oligopeptide including a C-terminal thioester, the second oligopeptide including an N-terminal cysteine having an unoxidized sulfhydryl side chain; then

Step B: condensing the unoxidized sulfhydryl side chain of the N-terminal cysteine with the C-terminal thioester for producing an intermediate oligopeptide linking the first and second oligopeptides with a  $\beta$ -aminothioester bond; and then

Step C: rearranging the  $\beta$ -aminothioester bond of the intermediate oligopeptide of said Step B for producing the oligopeptide product linking the first and second oligopeptides with an amide bond.

- 2. A method as described in Claim 1 wherein, in said step A, the catalytic thiol is selected from the group consisting of unconjugated mercaptans and conjugated thiols.
- 3. A method as described in Claim 2 wherein, in said step A, the catalytic thiol is benzyl mercaptan.

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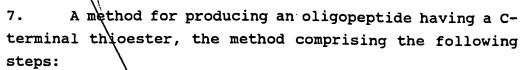




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- 4. A method as described in Claim 2 wherein, in said step A, the catalytic thiol is a conjugated thiol selected from the group consisting of thiophenol, 1-thio-2-nitrophenol, 2-thio-benzoic acid, 2-thio-pyridine, 4-thio-2-pyridinecarboxylic acid, and 4-thio-2-nitropyridine.
- 5. A method as described in Claim 4 wherein, in said step A, the conjugated thiol is thiophenol.
  - 6. An oligopeptide intermediate comprising:
  - a first oligopeptide segment having a C-terminal thioester,
  - a second oligopeptide segment having a N-terminal cysteine, and
  - a  $\beta$ -aminothioester linkage unit linking the C-terminal thioester and the N-terminal cysteine, said  $\beta$ -aminothioester linkage unit spontaneously rearranging intramolecularly to form an amide bond linking said first and second oligopeptides segments end to end.





Step A: providing a resin having a linker with an unoxidized thiol;

Step B: providing a Boc-amino acid succinimide ester; then

Step C:: admixing the resin of said Step A and the Bocamino acid succinimide ester of said Step B under reaction conditions for producing a Bocamino thioesterresin; then

Step D: assembling an oligopeptide onto the Boc-amino thioester-resin by stepwise solid phase peptide synthesis; then

Step E: cleaving the Boc-amino thioester-resin of said Step D with HS for producing an oligopeptide having a Cterminal thiol; and then

Step F: converting the oligopeptide having a C-terminal thiol of said Step E to the oligopeptide having a C-terminal thioester.

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